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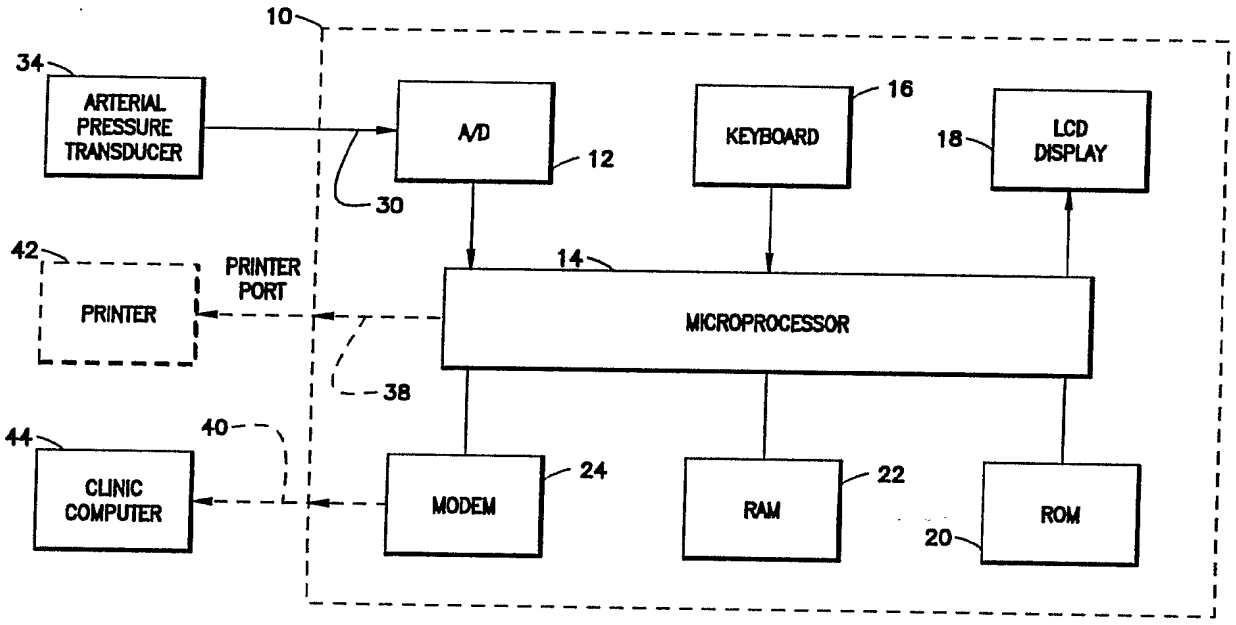
(54) Title: METHOD AND APPARATUS FOR MEASURING CARDIAC OUTPUT



(57) Abstract

Apparatus for measuring stroke volume/cardiac output includes a transducer (34) for measuring arterial blood pressure waveform, a digitizer (12) for digitizing the analog signal generated by the transducer (34) and a digital signal processor (14, 20, 22) for determining ejection time and heart rate. Processor circuitry (14) determines cardiac output using the ejection time, heart rate, the body surface area and age of the patient, with the cardiac output measure being displayed by the meter (18).

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METHOD AND APPARATUS FOR MEASURING CARDIAC OUTPUT

Technical Field of the Invention

The present invention pertains generally to the field of medicine, and more particularly to cardiology and biomedical engineering.

Background of the Invention

Cardiac output is an important hemodynamic variable widely used in the field of cardiology for diagnosis and other characterizations of the cardiovascular system. It is routinely used as a diagnostic measure of cardiac function, particularly in the diagnosis of congestive heart failure and related cardiac disease. Characterizations of the cardiovasculature using the Windkessel model, employed to obtain measures of vascular compliance, also require a measure of cardiac output.

Thermodilution and dye dilution procedures are considered two of the most accurate measures of cardiac output. They are, however, surgically invasive procedures which require catheterization of the subject. As such, these procedures are inconvenient, time consuming and expensive, as well as undesirable from the patient's perspective. Moreover, notwithstanding the fact that they are considered the most accurate measures of cardiac output, they have a reproducibility of only between ten to twenty percent. Other measures of cardiac output include: "eyeball" estimates, made on the basis of the patients size and subject to considerable error; Doppler measurement techniques which measure blood velocity and calculate output based on a further measure of aorta cross section, and which are time consuming and subject to errors in aorta cross section measurement; and rebreathing techniques, which are considered difficult to implement, and subject to considerable error if not executed with great care. The Minnesota Thoracic Impedance method, a non-invasive

measure of cardiac output, is another alternative measure. While this method may be adequate for detecting changes in cardiac output, it is poor at measuring the absolute value of cardiac output.

Others have devised procedures for measuring cardiac output based on measurements of body surface area, age, heart rate, weight, height and ejection time, whereby a quick, non-invasive measure of cardiac output can be obtained. For example, Smulyan et al., in "An Evaluation of the Cardiac Index," disclose a method for measuring cardiac output using a subject's height and weight (factors closely related to body surface area); Krovetz and Goldbloom, in "Normal Standards for Cardiovascular Data - I. Examination of the Validity of Cardiac Index," disclose a method using age, height, weight and heart rate; and Weissler et al., in "Relationships Between Left Ventricular Ejection Time, Stroke Volume, and Heart Rate in Normal Individuals and Patients with Cardiovascular Disease," establish some correlation between ejection time and cardiac output. While these procedures are relatively fast and easy compared to others, and thus are indicated over the slower, more cumbersome and invasive procedures, they are generally less accurate measures of cardiac output. The present invention provides a measure of cardiac output, in the genre of these procedures, with acceptable accuracy for many applications.

Summary of the Invention

According to the apparatus of the invention, there is provided a cardiac output meter having transducer means for measuring the blood pressure waveform of the patient and generating a corresponding analog signal, means for digitizing the analog signal generated by the transducer means, means for determining, by digital signal processing of the digitized blood pressure waveform, the ejection time and

heart rate, and means for calculating and displaying a measure of cardiac output based on the heart rate, ejection time, and the patient's body surface area and age.

According to another aspect of the meter, there is included means for automatically determining the body surface area by standard formula or nomogram, based on input variables including the subject's height and weight.

According to the method of the present invention, there is measured, either noninvasively or invasively, an arterial blood pressure waveform. The waveform data are processed to determine the ejection time of the heart. The heart rate is measured, and body surface area is determined by standard formula or by nomogram, using the subject's height and weight. Stroke volume is then determined in accordance with the following formula:

$$SVA = -6.6 + 0.25 \times ET + 40.4 \times BSA - 0.51 \times Age - 0.62 \times HR,$$

where SVA equals stroke volume in ml/beat, ET is ejection time in msec, BSA is body surface area in square meters, Age is the age of the subject, and HR is heart rate (beats per minute). Cardiac output is determined by multiplying SVA times the heart rate HR.

The present invention thus provides method and apparatus for determining cardiac output without special instrumentation beyond that normally required for hemodynamic monitoring or vascular compliance determination. The invention requires no calibration, is easily applied, can be done noninvasively, and, even if done invasively, is much simpler than the standard dilution technique. The invention thus has considerable potential for use in screening subjects based on stroke volume/cardiac output determinations.

Brief Description of the Drawings

Figure 1 is a schematic block diagram of the cardiac output meter according to the present invention;

Figure 2A and 2B comprise a schematic flow chart of the software of the present invention;

Figure 3 is illustrative example of typical arterial pulse contours in healthy patients;

Figure 4 is illustrative example of typical arterial pulse contours in diseased patients;

Figure 5 is a scatterplot of invasively measured stroke volume using thermal dilution vs. stroke volume obtained from the present invention for 71 cases which formed the basis for the development of the present invention; and

Figure 6 is a scatterplot of invasively measured stroke volume using thermodilution vs. stroke volume measured using the present invention for 39 separate, independent cases used to test the accuracy of the meter of the present invention.

Detailed Description of the Invention

The cardiac output meter 10 according to the present invention is shown in schematic block diagram form in Fig. 1. The meter 10 includes an analog to digital convertor (A/D) 12, preferably 12-bit, a microprocessor unit 14, for instance a 30386 model by Intel, a keyboard input 16, display 18, ROM 20, RAM 22 and modem 24. An input port 30 is provided to receive analog signal input from an arterial pressure transducer 34. A printer output port 38 and a telephone port 40 are provided from microprocessor 14 and modem 24, respectively.

Where the arterial waveform is obtained invasively, transducer 34 is preferably a Statham P23Db pressure transducer, connected to a brachial artery by an 18-gauge, 2-inch Teflon catheter. This catheter-transducer system has an undamped natural frequency

higher than 25 HZ and a damping coefficient less than 0.5, providing an acceptable frequency response. It shall be understood, however, that while the brachial artery is preferred, other arterial peripheral locations for obtaining the pulse pressure contour can be substituted.

A non-invasive transducer 34 unit can also be used, for example, a finger-cuff transducer unit using a counter pulsation technique wherein the waveform is detected by balancing the pressure in the finger cuff with that in the finger. A commercially available finger-cuff transducer unit is the Finapres® Continuous NIBP Monitor Model 2300, from Ohmeda Monitoring Systems division of the BOC Group, Inc., 355 Inverness Drive South, Engelwood, Colorado 80112-5810. The Finapres® device produces an analog output signal which is equivalent to the output signal of the P23Db pressure transducer, and can be fed through port 30 to A/D converter 12. Another non-invasive transducer unit acceptable for use with the present invention is the Model 506 Non-invasive Patient Monitor from Criticare Systems, Inc., 20900 Swenson Drive, Suite 398, Waukesha, Wisconsin 53186.

The software component 50 of the meter 10 is illustrated in block diagram flow-chart form in Figs. 2A and B. Software within meter 10 is preferably maintained in ROM 20 and is referenced by microprocessor 14. Alternatively, software 50 can be stored in magnetic or other digital form on a floppy computer disk or equivalent connected so as to be accessed by the microprocessor.

Software 50 runs on microprocessor 14 to control the acquisition of arterial pressure pulse data, and to perform other meter functions, as described below. An initialization and mode select routine 52 is provided for initializing microprocessor 14, including prompting the user to enter patient information,

including the patient's age, height (in centimeters) and weight (in kilograms), and/or body surface area (in square meters). Routine 52 further allows either the meter mode or communication mode to be selected. If the meter mode is selected, A/D convertor 12 is activated (54) to digitize an analog pressure pulse signal generated by transducer 34. Figs. 3 and 4 illustrate typical brachial artery pulse pressure contours for normotensive and hypertensive patients, respectively.

The present invention uses an A/D sampling rate of 200 samples/second, which is satisfactory to capture the highest frequency components of interest in the pressure pulse. It shall be understood, however, that higher or lower sampling rates may be used, and that the invention is in no way limited to the 200 samples/second rate. Routine 56 provides that the artery is metered for approximately 30 seconds, producing in the range of 25 to 60 digitized pulses, depending on the heart rate. The stream of digitized pulses are stored in RAM 22 in the form of a continuous series of periodic time dependent data byte samples, with each data byte corresponding to the instantaneous pressure of the artery.

Routine 60 determines body surface area by standard formula, or alternatively looks it up in a nomogram table stored in memory, using the patient's height and weight data. Alternatively, body surface area can be determined by the physician or other care giver and entered into the meter at routine 52, as noted above. A formula for determining BSA known to work in connection with the present invention is:

$$BSA\ (m^{-2}) = 0.0072 \times weight^{0.425} \times height^{0.725}$$

where weight is in kilograms and height is in centimeters.

A nomogram table known to work with the present invention is found in the Merck Manual, 12th edition,

1972 on page 1840 (reproduced from Wm. Brothby and R. B. Sandford, Boston Medical and Surgical Journal, Vol. 185, p. 337, 1921).

Selection routine 70 analyzes the recorded wave data to determine ejection time. First, routine 70 selects a group of consecutive representative beats (it has been found that six to ten beats are preferred but the number used is in no way critical to the invention) preferably of comparatively low noise content. Representative beats are identified by establishing windows of permissible heart rate and mean arterial pressure values whereby abnormally fast or slow heartbeats, or high or low pressures can be rejected. The routine can thus pick the series of beats which is most representative. The heart rate (HR) is also determined by this routine, by counting the number of beats per unit time. Where possible it is preferable that the windows be tailored to the patient, thus allowing more precise selection of representative beats.

Routine 70 determines ejection time as follows. First, the heart waveforms are marked for analysis. When marked manually, a clinician can identify the onset of systole and the upstroke, by correlating to the first heart sound S_1. The end of systole, signalled by diastole, can be found manually by correlating to the second heart sound S_2. Ejection time is then determined by the time between the occurrence of systole to diastole. For example, in Figs. 3 and 4 ejection time is marked by the respective segments A and B, assuming a waveform obtained proximate the heart.

The present invention uses a software analysis algorithm at routine 70 to predict and select the segment in each wave most probably corresponding to ejection time. Routine 70 searches the waveform data for the waveform upstroke marking systole, and then for the dicrotic notch (D), looked for after the peak of the systolic upstroke, and marks the onset of diastole just

before the location of the dicrotic notch on the wave. The ejection time (ET) is then determined from the location of the onset of systole and diastole. Transit time effects due to the distance between the aorta and the measurement site are taken into account in the ejection time measurement by moving back a predetermined interval (depending on where with arterial waveform is measured in the arterial system) from the trough of the dicrotic notch to determine end of systole for the purposes of this ejection time determination. The ejection time is thus the time between the upstroke (beginning of systole) and this point marking the end of systole. For waveforms obtained from the femoral artery, an interval of 25 milliseconds has been found satisfactory to compensate for transit time effects. Shorter or longer intervals would be appropriate for waveforms obtained closer to or further from the heart, respectively.

Alternatively, device 10 can include means for digitizing an analog signal representing the heart sounds, software for identifying the first and second heart sounds S_1 and S_2, and for correlating them to the digitized arterial waveform to identify the onset of systole and diastole.

Routine 71 calculates stroke volume using the following formula:

$$SVA = -6.6 + (0.25 \times ET) + (40.4 \times BSA) - (0.51 \times Age) - (0.62 \times HR),$$

where SVA equals stroke volume in ml/beat, ET is ejection time in msec, BSA is body surface area in square meters and HR is heart rate (bpm);

using the heart rate (HR), body surface area (BSA), ejection time (ET) and age for the subject. Cardiac output can be determined by multiplying heart rate (HR) times stroke volume (SVA).

Routine 72 is provided to indicate via display 18 the calculated value, either graphically, for instance a bar graph showing the magnitude of cardiac output or stroke volume on a scale, or by displaying a corresponding numerical value, on the LCD display. Routine 80 is provided to report the analysis results on an optional printer 42.

Meter 10 also includes communications capability, whereby the measured cardiac output data (or, if desired other stored vascular parameters) may be communicated to further computer equipment 44 in a clinic or hospital, such as a personal computer or minicomputer. Accordingly, meter 10 may be used by a patient at home with measured cardiac output being transmitted back to a treating hospital or clinic for review or for further analysis. For this purpose software 50 provides a communications mode including routines 145 and 146, which provide for establishing a communication link with remote system and for downloading the cardiac output measurement.

As shown in Figure 1, a clinic or hospital computer 44 is provided to communicate with meter 10 using a standard modem-telephone link. Figure 2B illustrates in diagrammatic form the software 150 provided for clinic computer 44. A routine 152 is provided for establishing the communication link with meter 10. Computer 44 preferably includes an auto-answer modem so that meter 10 may establish communication therewith with a minimum of effort. Data acquisition routine 154 is provided to receive one or more cardiac output values, which may be stored in RAM 22. Report/display routine 156 provides reporting or display of downloaded cardiac output values for use by the hospital or clinic staff.

Figure 5 is a scatterplot of invasively measured stroke volume (in ml/heart beat) using thermodilution (the "Gold Standard") vs. stroke volume

(in ml/heart beat) measured using the meter of the present invention, for 71 cases. These 71 cases formed the basis for development of the present invention, which included a multiple linear regression fit. Figure 5 shows that in 90% of the cases, there was less than a (+-)25% difference between the cardiac output measurement obtained by thermodilution and that obtained using the present invention.

Figure 6 is a scatterplot of invasively measured stroke volume (in ml/heart beat) using thermodilution (the "Gold Standard") vs. stroke volume (in ml/heart beat) measured using the meter of the present invention, for 39 separate, independent cases. The subjects of this study ranged from 19-75 in age. Figure 6 shows that in 88% of the cases, there was less than a (+-)25% difference between the cardiac output measurement obtained by thermodilution and that obtained using the present invention. The accuracy of the meter, as currently understood from the cases against which it has been tested, is thus adequate to provide a cardiac output measure adequate for many applications wherein an approximate measure is acceptable. This accuracy compares favorably against the 10-20% reproducibility of the most accurate dilution techniques.

The present invention also includes a method for measuring stroke volume/cardiac output. The method includes the following steps:

1) Measuring, either noninvasively or invasively, an arterial blood pressure waveform, from which the ejection time of the heart is determined, taking into account transit time effects between the aorta and the measurement site;
2) Measuring the heart rate;
3) Determining the body surface area by standard formula or by nomogram, using the subject's height and weight;

4) Determining stroke volume substantially in accordance with the following formula: SVA = -6.6 + 0.25 x ET + 40.4 x BSA - 0.51 x Age -0.62 x HR, where SVA equals stroke volume in ml/beat, ET is ejection time in msec, BSA is body surface area in square meters and HR is heart rate (bpm); and

5) Calculating cardiac output by multiplying heart rate HR times stroke volume (SVA).

It is currently contemplated that the formula for determining cardiac output set forth herein will be further refined and adjusted as further data is collected and/or as adjustments to constants and factors are determined to produce more accurate determinations of cardiac output. The formula may be adjusted by performing a multiple linear regression to fit a new formula on "Gold Standard" data. Accordingly, it shall be understood that the basic structure of the formula is to be emphasized. Also, it shall be understood that both cardiac output per se (SVA X heart rate) and SVA are considered measures of cardiac output for the purpose of the claims appended hereto. Moreover, it is contemplated that many changes and modifications may be made to the method and apparatus of the invention without departing from the spirit and scope of the claims appended hereto.

In the claims:

1. A cardiac output meter, comprising:

a) transducer means for measuring an arterial blood pressure waveform of a human patient and generating a corresponding analog signal;

b) means for digitizing the analog signal generated by the transducer means;

c) means for determining, by digital signal processing of the digitized blood pressure waveform, the ejection time and heart rate;

d) means for determining a measure of cardiac output using the ejection time, heart rate and body surface area and age of the patient; and

e) means for indicating said measure of cardiac output.

2. The meter of claim 1 further wherein said means for determining includes means for determining stroke volume substantially in accordance with the following formula:

$$SVA = -6.6 + 0.25 \times ET + 40.4 \times BSA - 0.51 \times Age - 0.62 \times HR,$$

where SVA equals stroke volume in ml/beat, ET is ejection time in msec, BSA is body surface area and HR is heart rate (bpm).

3. The meter of claim 1 further wherein said means for indicating comprises means for displaying a bar graph of the magnitude of cardiac output.

4. A method of determining cardiac output in a human patient, comprising:

a) measuring an arterial blood pressure waveform and determining therefrom the ejection time of the heart;

b) measuring the heart rate;

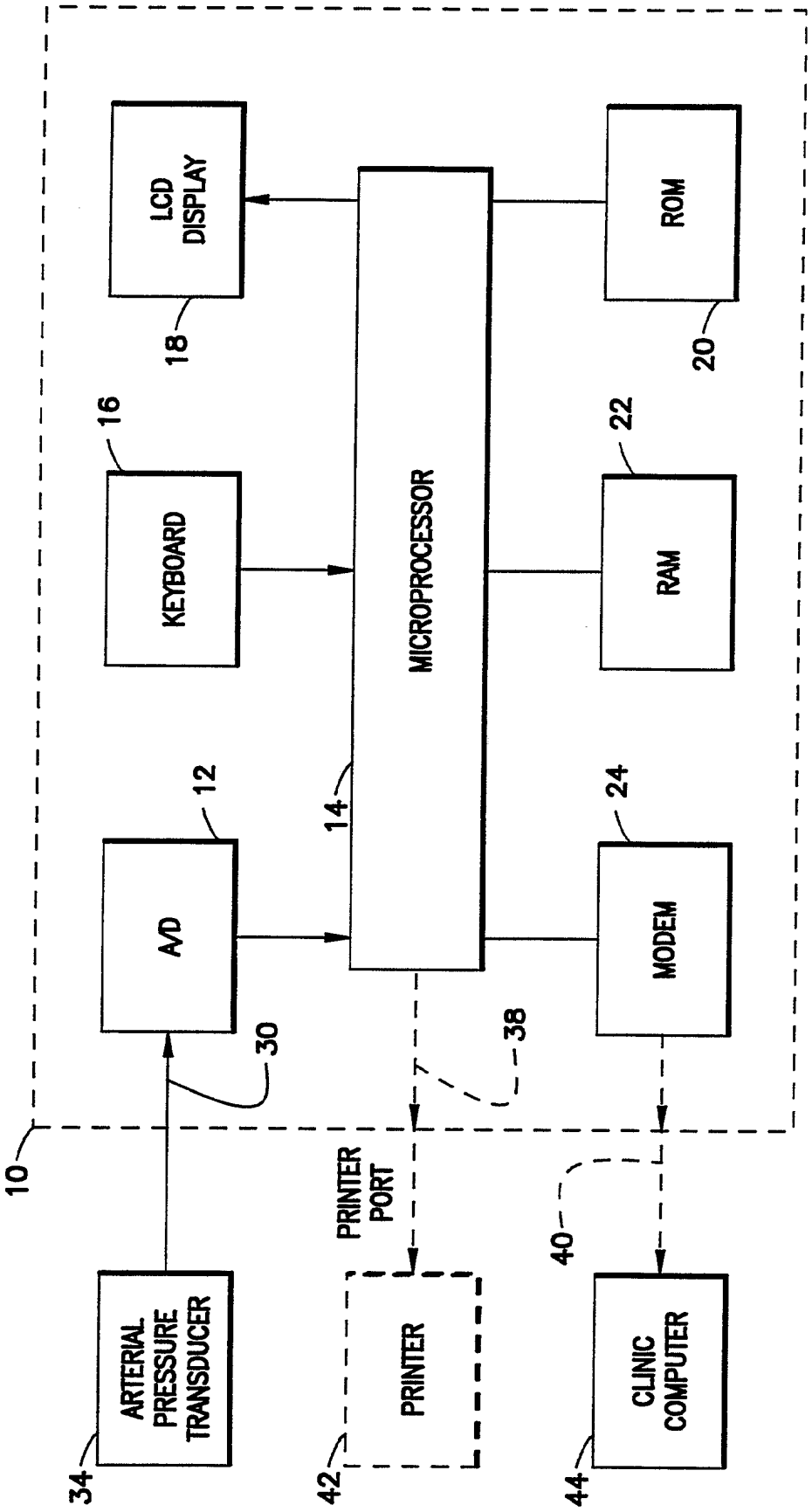
c) determining the body surface area; and

d) determining a measure of cardiac output of the patient substantially in accordance with the ejection time, age, body surface area and heart rate of the patient.

5. The method of claim 4 wherein said determining of cardiac output is determined substantially in accordance with the following formula:

$$SVA = -6.6 + 0.25 \times ET + 40.4 \times BSA - 0.51 \times Age - 0.62 \times HR,$$

where SVA equals stroke volume in ml/beat, ET is ejection time in msec, BSA is body surface area and HR is heart rate (bpm).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ROM
20
16
KEYBOARD
MICROPROCESSOR
22
RAM
12
A/D
14
24
MODEM
30
38
10
PRINTER PORT
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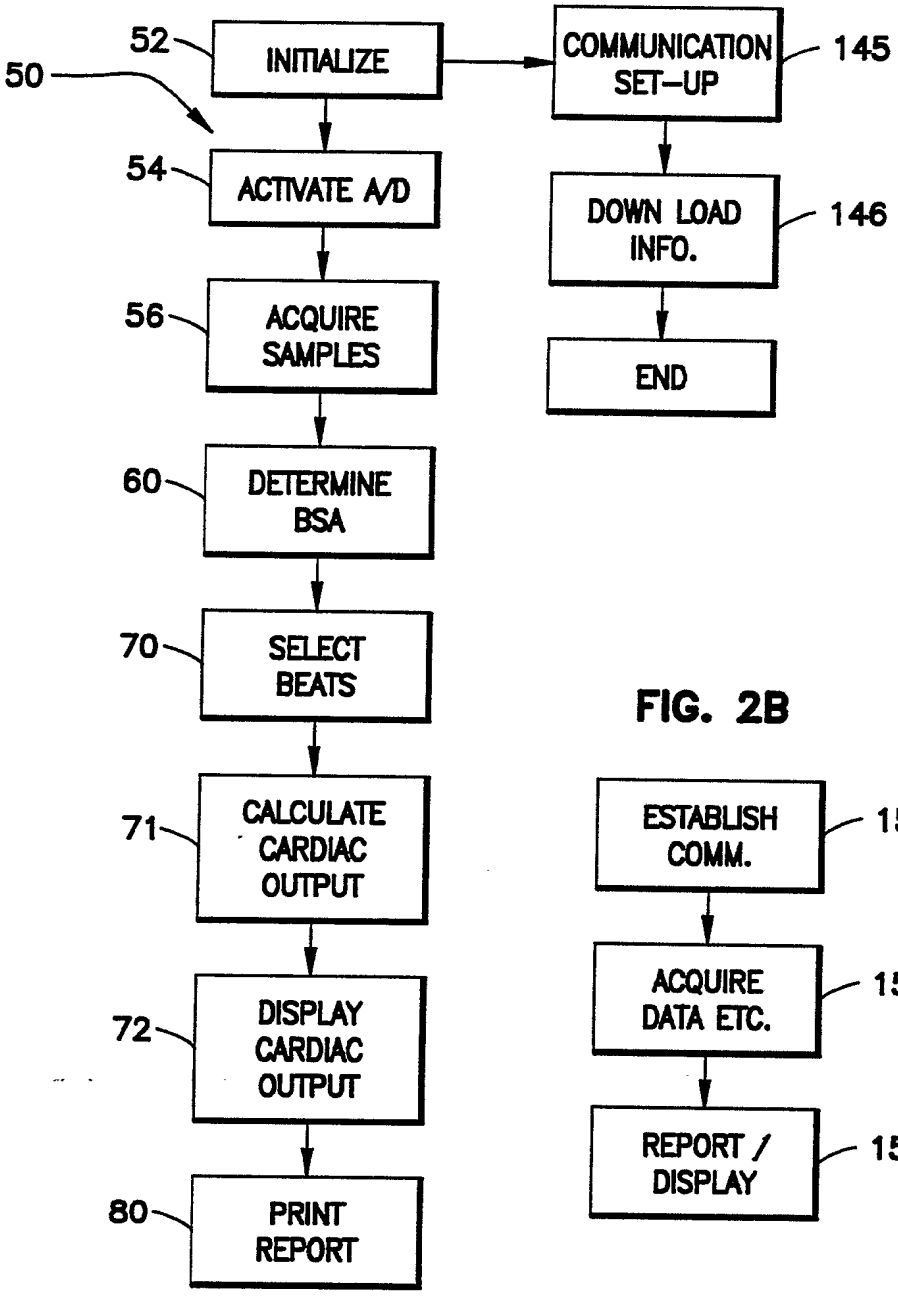
ARTERIAL PRESSURE TRANSDUCER
34
PRINTER
42
CLINIC COMPUTER
44

FIG. 1

FIG. 2A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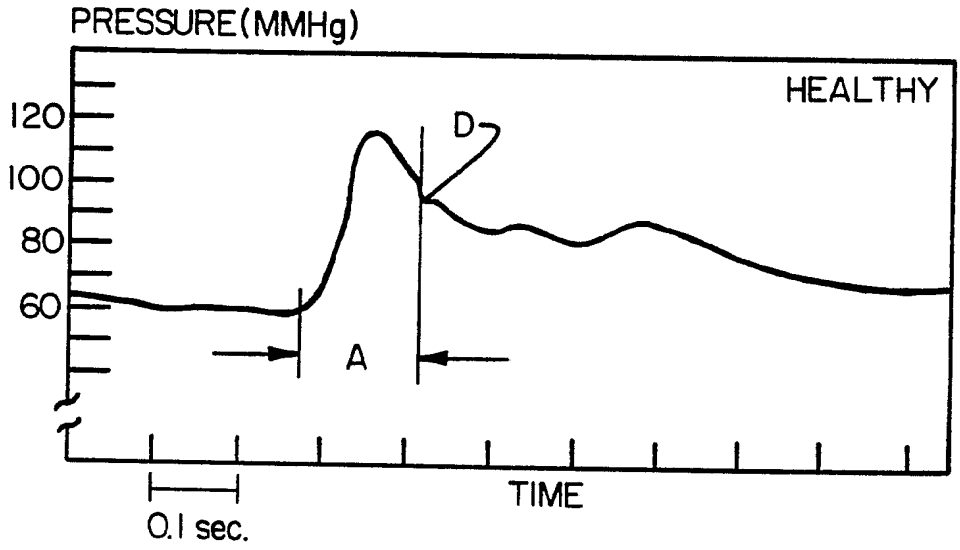
52
INITIALIZE
54
ACTIVATE A/D
56
ACQUIRE SAMPLES
60
DETERMINE BSA
70
SELECT BEATS
71
CALCULATE CARDIAC OUTPUT
72
DISPLAY CARDIAC OUTPUT
80
PRINT REPORT
COMMUNICATION SET-UP
145
DOWN LOAD INFO.
146
END

FIG. 2B

ESTABLISH COMM.
152
ACQUIRE DATA ETC.
154
REPORT / DISPLAY
156

FIG. 3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100
80
60
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A
TIME
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FIG. 4

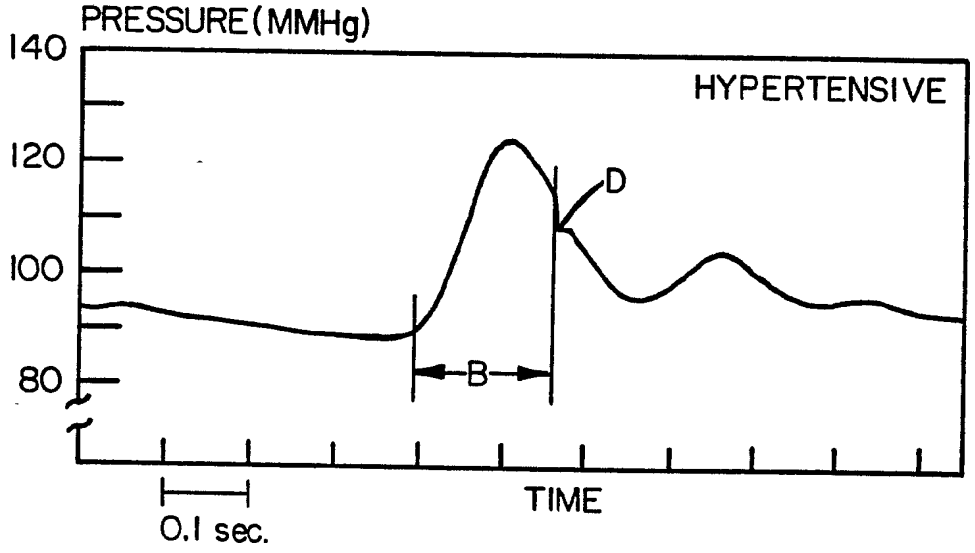
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FIG. 5

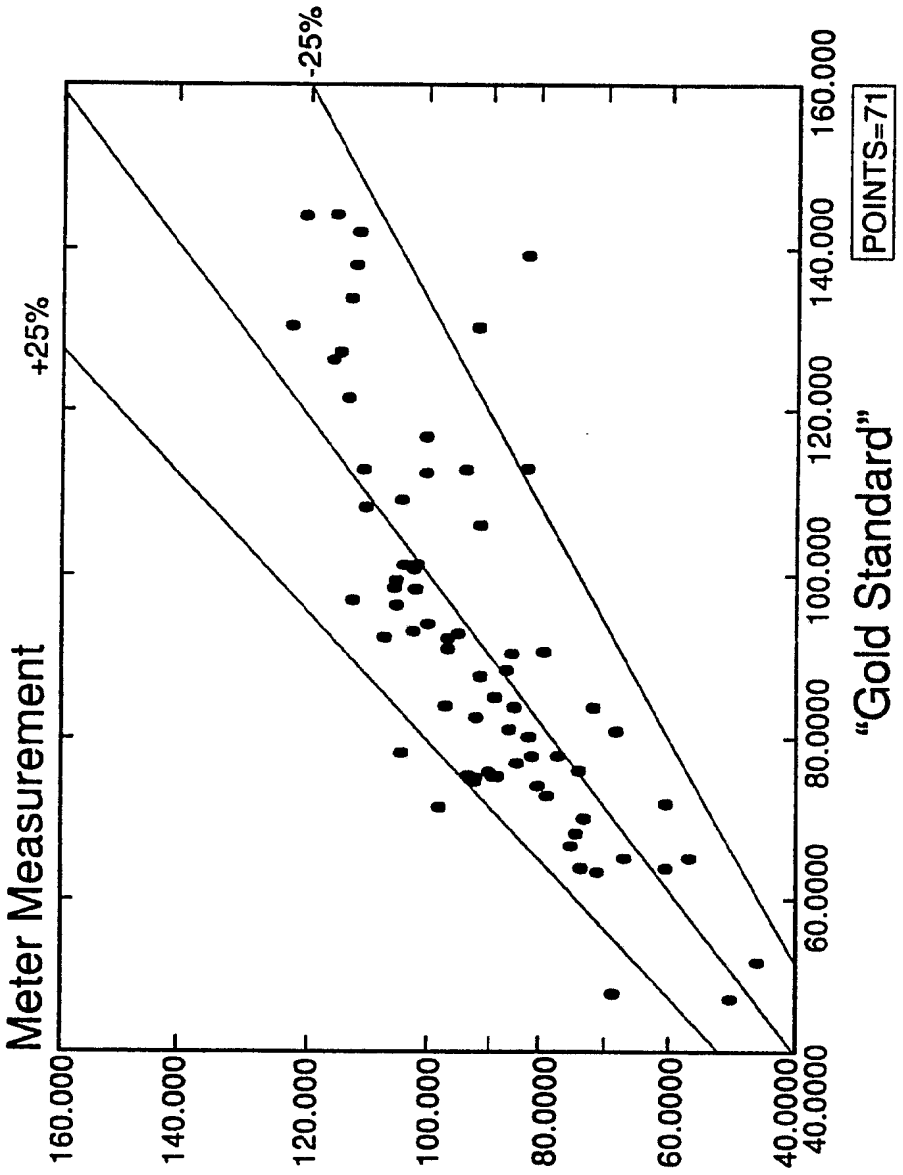
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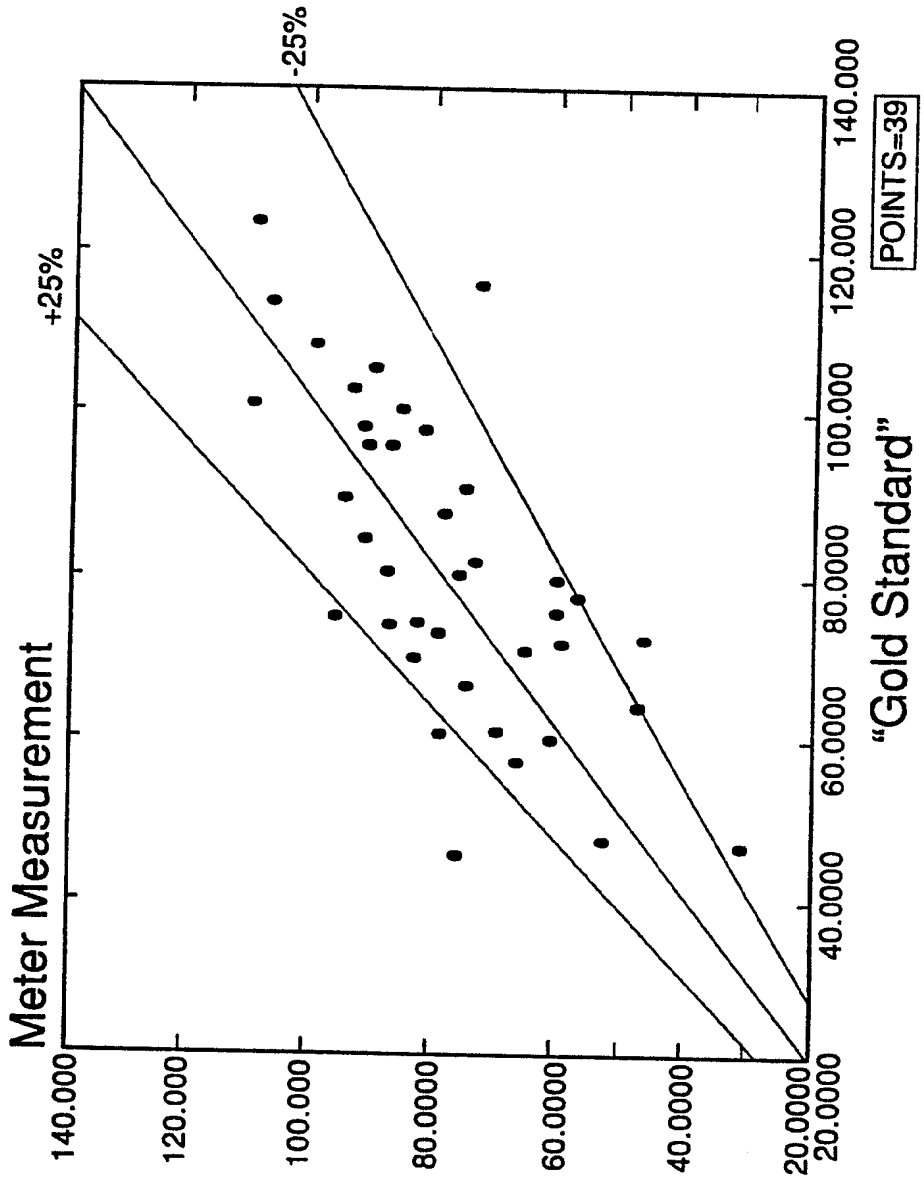
FIG. 6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20.0000
40.0000
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100.000
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INTERNATIONAL SEARCH REPORT

International Application No. PCT/US91/07523

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) [6]

According to International Patent Classification (IPC) or to both National Classification and IPC

IPC(5): A61B 5/024

U.S. CL.: 128/713

II. FIELDS SEARCHED

Minimum Documentation Searched [7]

Classification System	Classification Symbols
US	128/672,673,687-689,713

Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched [8]

III. DOCUMENTS CONSIDERED TO BE RELEVANT [9]

Category *	Citation of Document, [11] with indication, where appropriate, of the relevant passages [12]	Relevant to Claim No. [13]
A	US, A, 4,137,910 (MURPHY) 06 February 1979, See abstract.	
A	US, A, 4,562,843 (DJORDJEVICH) 07 January 1986, See abstract.	
A	US, A, 4,807,638 (SRAMEK) 28 February 1989, See abstract.	
A	Circulation, Volume 46, issued September 1972, Edwin L. Alderman et al., "Evaluation of the Pulse-Contour Method of Determining Stroke Volume in Man", See pages 546-558.	
A	European Heart Journal, 4 issued 1983, T. Tajimi et al., "Evaluation of pulse Contour Methods in Calculating Stroke Volume from Pulmonary Artery Pressure Curve (Comparison with Aortic Pressure Curve)", See pages 502-511.	

* Special categories of cited documents: [10]

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

IV. CERTIFICATION

Date of the Actual Completion of the International Search

06 February 1992

Date of Mailing of this International Search Report

09MAR 1992

International Searching Authority

ISA/US

Signature of Authorized Officer

KEVIN PONTIUS

FURTHER INFORMATION CONTINUED FROM THE SECOND SHEET

V. [X] OBSERVATIONS WHERE CERTAIN CLAIMS WERE FOUND UNSEARCHABLE [1]

This international search report has not been established in respect of certain claims under Article 17(2) (a) for the following reasons:

1. [X] Claim numbers 1-5, because they relate to subject matter [12] not required to be searched by this Authority, namely:

Claims 1-5 are drawn to a mathematical algorithm and thus, are not statutory subject matter.

2. [ ] Claim numbers ....., because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out [13], specifically:

3. [ ] Claim numbers _____, because they are dependent claims not drafted in accordance with the second and third sentences of PCT Rule 6.4(a).

VI. [ ] OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING [2]

This International Searching Authority found multiple inventions in this international application as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims of the international application.

2. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims of the international application for which fees were paid, specifically claims:

3. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claim numbers:

4. [ ] As all searchable claims could be searched without effort justifying an additional fee, the International Searching Authority did not invite payment of any additional fee.

Remark on Protest

[ ] The additional search fees were accompanied by applicant's protest.

[ ] No protest accompanied the payment of additional search fees.